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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/776,934	02/10/2004	Bo Hansen	58610 (71432)	2105

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EXAMINER	
CHONG, KIMBERLY	
ART UNIT	**PAPER NUMBER**
1635	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/776,934	HANSEN ET AL.	
	Examiner	Art Unit	
	Kimberly Chong	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *19-21,160-169* is/are allowed.

6)☒ Claim(s) *3,6-8,10-13,15,16,19-21,23-31,33,35-38,45,46,48-52,120-124 and 153-159* is/are rejected.

7)☒ Claim(s) *153* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02814/2004, 10/12/2007* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 3,6-8,10-13,15,16,19-21,23-31,33,35-38,45,46,48-52,120-124 and 153-169.

DETAILED ACTION

Status of Application/Amendment/Claims

Applicant's response filed 10/12/2007 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 4/17/2007 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

With entry of the amendment filed on 10/12/2007, claims 3, 6-8, 10-13, 15-16, 19-21, 23-31, 33, 35-38, 45-46, 48-52, 120-124 and 153-169 are pending and currently under examination. Applicant has canceled claims 4-5, 9, 14, 17-18, 22, 32, 34, 39-44, 47, 53-119 and 123-152.

New Claim Objections and Rejections

Claim Objections

Claim 153 is objected to for the following reasons: The claim recites the compound comprises a subsequence of *at least 8 nucleotide analogues* and wherein said subsequence comprises at least *one nucleotide analogue*. Clarification is required to discern the minimum number of nucleotide analogues the subsequence comprises.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6-8, 10-12 and 35-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 6-8 and 10 are indefinite because they depend from canceled claim 5 and therefore it is unclear what further limitations would be encompassed in the claims.

Claims 11 and 12 are indefinite because they depend from canceled claim 9 and therefore it is unclear what further limitations would be encompassed in the claims.

Claims 35-38 are indefinite because they depend from canceled claim 34 and therefore it is unclear what further limitations would be encompassed in the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 23-31, 33, 45-46, 120-124 and 153-154 are rejected under 35 U.S.C. 102(b) as being anticipated by Bennett et al. (U.S. Patent No. 6,077,709).

The claims are drawn to a compound consisting of 12-50 nucleotides and/or nucleotide analogues wherein said compound comprise a subsequence of at least 8 nucleotides or nucleotide analogues, said subsequence being located within the sequence having SEQ ID No. 130 and wherein said subsequence comprises at least one nucleotide analogue or up to 8 nucleotide analogues, wherein the analogues is selected from a group as listed in claim 154, such as a 2'-methoxyethyl, wherein the compound comprises a conjugate and a pharmaceutically acceptable carrier and wherein the composition further comprises a chemotherapeutic agent such as methotrexate.

Bennett et al. teach an antisense compound targeted to a survivin gene wherein the compound is 18 nucleobases in length comprising a subsequence of at least 8 nucleotides of SEQ ID No. 130 (see Table 1, SEQ ID NO. 1). For purposes of prior art, the claims are given their broadest reasonable interpretation in light of the specification and the limitation "comprises a subsequence of at least 8 nucleotides or nucleotide analogues, said subsequence being located with the sequence ctcaatccatggcagc (SEQ ID NO. 130) can be interpreted to mean the subsequence comprises 8 nucleotides, of any order or configuration as listed in SEQ ID No. 130. The claims and the instant specification do not limit the scope of the subsequence to comprise 8 nucleotides in consecutive order or that the 8 nucleotides be contiguous nucleotides of SEQ ID NO. 130. Therefore. SEQ ID No. 1 of Bennett et al. meets the limitation of claim 153. Bennett et al. further teach the antisense compound can comprise analogues such as 2'-methoxyethyl and phosphate and phosphorothioate internucleoside linkages (see

columns 7-8). Bennett et al. further teach compositions comprising pharmaceutically acceptable carriers or diluents (see column 10) and teach the composition can be attached to a conjugate such as fatty acids and penetration enhancers (see column 12) and further teach the composition further comprises chemotherapeutic agents such as methotrexate wherein the compounds can be used as therapeutic molecules (see column 15). A specific embodiment exemplifying an antisense compound comprising at least 8 nucleotide analogues such as a chimeric antisense compound is shown in Example 16.

Thus, Bennett et al. anticipates claims 23-31, 33, 45-46, 120-124 and 153-154 of the instant invention.

Claims 23-31, 33, 45-46, 121 and 153 are rejected under 35 U.S.C. 102(e) as being anticipated by Draper et al. (U.S. Patent No. 6,310,044).

> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

The claims are drawn to a compound consisting of 12-50 nucleotides and/or nucleotide analogues wherein said compound comprise a subsequence of at least 8 nucleotides or nucleotide analogues, said subsequence being located within the sequence having SEQ ID No. 130 and wherein said subsequence comprises at least one nucleotide analogue or up to 8 nucleotide analogues, and wherein the compound comprises a pharmaceutically acceptable carrier..

Draper et al. teach an oligonucleotide compound comprising at least 8 nucleotides of SEQ ID No. 130 (see attached sequence alignment and SEQ ID No. 4 of Draper et al.). Draper et al. teach the oligonucleotide compound comprises from 6 to 50 nucleotide analogues (see column 11) and teach the oligonucleotide comprises phosphate and can comprise all phosphorothioate internucleotide linkages (see columns 10-11 and Table 10, column 26). Draper et al. further teach compositions comprising pharmaceutically acceptable carriers (see column 12, lines 9-18).

Thus, Draper et al. anticipates claims 23-31, 33, 45-46,121 and 153 of the instant invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 23-31, 33, 45-46, 48-52, 120-124, 153-159 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bennett et al. (U.S. Patent No. 6,077,709), in view of Koch et al. (US 2003/0032794) and Kurreck et al. (Nucleic Acids Research, 2002, Vo. 30, No. 9: 1911-1918).

The claims are drawn to a compound consisting of 12-50 nucleotides and/or nucleotide analogues wherein said compound comprise a subsequence of at least 8 nucleotides or nucleotide analogues, said subsequence being located with the sequence having SEQ ID No. 130 and wherein said subsequence comprises at least one nucleotide analogue, wherein the analogues is selected from a group as listed n claim 154, wherein the compound comprises a sequence having beta-D-oxy-LNA and phosphorothioate linkages ad claimed in the configuration as claimed in claims 48-52.

Bennett et al. teach an antisense compound targeted to a survivin gene wherein the compound is 18 nucleobases in length comprising a subsequence of at lest 8 nucleotides of SEQ ID No. 130 (see Table 1, SEQ ID NO. 1). For purposes of prior art, the claims are given their broadest reasonable interpretation in light of the specification and the limitation "comprises a subsequence of at least 8 nucleotides or nucleotide analogues, said subsequence being located with the sequence ctcaatccatggcagc (SEQ ID NO. 130) can be interpreted to mean the subsequence must comprise 8 nucleotides, of any order or configuration as listed in SEQ ID No. 130. The claims and the instant specification do not limit the scope of the subsequence to comprise 8 nucleotides in consecutive order or that the 8 nucleotides be contiguous nucleotides of SEQ ID NO. 130. Therefore. SEQ ID No. 1 of Bennett et al. meets the limitation of claim 153.

Bennett et al. further teach the antisense compound can comprise analogues such as 2'-methoxyethyl, phosphate and phosphorothioate internucleoside linkages (see columns 7-8). Bennett et al. further teach compositions comprising pharmaceutically acceptable carriers or diluents (see column 10) and teach the composition can be attached to a conjugate such as fatty acids and penetration enhancers (see column 12) and further teach the composition further comprises chemotherapeutic agents such as methotrexate and further teach the compound can be used as a therapeutic compound for the treatment of diseases (see columns 15-16). A specific embodiment exemplifying an antisense compound comprising at least 8 nucleotide analogues such as a chimeric antisense compound is shown in Example 16.

Bennett et al. does not teach antisense compounds comprising locked nucleic acids (LNA) wherein the LNA are thio-LNA, amino-LNA, oxy-LNA or beta-D-oxy-LNA and further do not teach the antisense compound comprises a stretch of 2-6 LNA followed by a stretch of 4-12 nucleotides which is followed by a stretch of 4 LNA.

Kurreck et al. teach antisense oligonucleotides comprising LNAs improves the affinity for complementary sequences and increase the stability of such oligonucleotides (see page 1912). Kurreck et al. teach incorporation of LNAs into oligonucleotides wherein the LNA are configured as gapmers, a stretch of 2-5 LNA, followed by a stretch of 8-14 nucleotides followed by a stretch of 2-5 LNA increase the oligonucleotide target affinity (see Table 1).

Koch et al. teach antisense compounds comprising LNA are promising new drug candidates and teach preparation of LNA such as amino-LNA and oxy-beta-D-LNA (see paragraph 0013-0014).

It would have been obvious to one of skill in the art to incorporate LNA, particularly LNA in a gapmer configuration as taught by Kurreck et al. and Koch et al. into the antisense oligonucleotide taught by Bennett et al.

One of skill in the art would have been motivated to incorporate LNA into the antisense oligonucleotide taught by Bennett et al. because Kurreck et al. teach LNAs improves the affinity for complementary sequences and increase the stability of such oligonucleotides. Further, one would have wanted to improve the target affinity of the antisense oligonucleotide taught by Bennett et al. given Bennett et al. teach the antisense oligonucleotide can modulate the expression of survivin gene expression which leads to a treatment of such diseases associated with overexpression from said gene, such as cancer. One would have been motivated to incorporate LNA in different configurations and as a matter of routine optimization design antisense oligonucleotide comprising LNA in different configurations including nucleotides in next to LNA in order to determine the most efficient configuration of antisense oligonucleotides comprising LNA that allow for maximum stability and target affinity. Moreover, one of skill in the art would have been motivated to specifically incorporate LNA, such as oxy-beta-D-LNA given Koch et al. teach this is a preferred LNA and teach synthesis of oligonucleotide comprises said LNA.

One would have been expected to be able to incorporate LNA into antisense compounds that allow for increased stability and target affinity given Kurreck et al. teach such compounds are capable of inhibition of gene expression and one of skill in the art would have expected to be able to synthesize LNA given Koch et al. details preparation of LNA and incorporation into oligonucleotides.

Thus in the absence of evidence to the contrary, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 23-31, 33, 45-46, 48-52, 120-124, 153-159 are rejected under 35 U.S.C. 103(a) as being unpatentable over Draper et al. (U.S. 6,310,044), Bennett et al. (U.S. Patent No. 6,077,709), Koch et al. (US 2003/0032794) and Kurreck et al. (Nucleic Acids Research, 2002, Vo. 30, No. 9: 1911-1918).

The claims are drawn to a compound consisting of 12-50 nucleotides and/or nucleotide analogues wherein said compound comprise a subsequence of at least 8 nucleotides or nucleotide analogues, said subsequence being located with the sequence having SEQ ID No. 130 and wherein said subsequence comprises at least one nucleotide analogue, wherein the analogues is selected from a group as listed n claim 154, wherein the compound comprises a sequence having beta-D-oxy-LNA and phosphorothioate linkages ad claimed in the configuration as claimed in claims 48-52 and 159-169.

Draper et al. teach an oligonucleotide compound comprising at least 8 nucleotides of SEQ ID No. 130 (see attached sequence alignment and SEQ ID No. 4 of Draper et al.). Draper et al. teach the oligonucleotide compound comprises from 6 to 50 nucleotide analogues (see column 11) and teach the oligonucleotide comprises phosphate and phosphorothioate internucleotide linkages (see columns 10-11 and Table 10, column 26). Draper et al. further teach compositions comprising pharmaceutically acceptable carriers (see column 12, lines 9-18). Draper et al. does not teach compounds comprising analogues such as 2'-methoxyethyl, conjugates and pharmaceutical compositions comprising chemotherapeutic agents.

Draper et al. further does not teach antisense compounds comprising locked nucleic acids (LNA) wherein the LNA are thio-LNA, amino-LNA, oxy-LNA or beta-D-oxy-LNA and further do not teach the antisense compound comprises a stretch of 2-6 LNA followed by a stretch of 4-12 nucleotides which is followed by a stretch of 4 LNA.

Bennett et al. teach antisense compound can comprise analogues such as 2'-methoxyethyl, phosphate and phosphorothioate internucleoside linkages (see columns 7-8). Bennett et al. further teach compositions comprising pharmaceutically acceptable carriers or diluents (see column 10) and teach the composition can be attached to a conjugate such as fatty acids and penetration enhancers (see column 12) and further teach the composition further comprises chemotherapeutic agents such as methotrexate and teach the compounds can be used in the treatment of diseases (see columns 15-16). A specific embodiment exemplifying an antisense compound

comprising at least 8 nucleotide analogues such as a chimeric antisense compound is shown in Example 16.

Kurreck et al. teach antisense oligonucleotides comprising LNAs improves the affinity for complementary sequences and increase the stability of such oligonucleotides (see page 1912). Kurreck et al. teach incorporation of LNAs into oligonucleotides wherein the LNA are configured as gapmers, a stretch of 2-5 LNA, followed by a stretch of 8-14 nucleotides followed by a stretch of 2-5 LNA increase the oligonucleotide target affinity (see Table 1).

Koch et al. teach antisense compounds comprising LNA are promising new drug candidates and teach preparation of LNA such as amino-LNA and oxy-beta-D-LNA (see paragraph 0013-0014).

It would have been obvious to one of skill in the art to make compounds comprising nucleotide analogues, such as 2'-methoxyethyl and compounds comprising conjugates and chemotherapeutic agents as taught by Bennett et al. It would have been further obvious to incorporate LNA, particularly LNA in a gapmer configuration as taught by Kurreck et al. and Koch et al. into the antisense oligonucleotide taught by Draper et al.

One of skill in the art would have been motivated and it would have been a mater of routine skill in the art to incorporate nucleotide analogues such as 2'-methoxyethyl and conjugates and chemotherapeutic agents into the compounds and compositions taught by Draper et al. for the purposes of increased stability of the compound and enhanced therapeutics when delivered to cells. One of skill in the art would have been

motivated to incorporate LNA into the antisense oligonucleotide taught by Draper et al. because Kurreck et al. teach LNAs improves the affinity for complementary sequences and increase the stability of such oligonucleotides. Further, one would have wanted to improve the target affinity of the antisense oligonucleotide taught by Draper et al. given Draper et al. teach the antisense oligonucleotide can modulate the expression of survivin gene expression which leads to a treatment of such diseases associated with overexpression from said gene, such as cancer. One would have been motivated to incorporate LNA in different configurations and as a matter of routine optimization design antisense oligonucleotide comprising LNA followed nucleotides in order to determine the most efficient configuration of antisense oligonucleotides comprising LNA that allow for maximum stability and target affinity. Moreover, one of skill in the art would have been motivated to specifically incorporate LNA, such as oxy-beta-D-LNA given Koch et al. teach this is a preferred LNA and teach synthesis of oligonucleotide comprises said LNA.

One would have been expected to be able to incorporate nucleotide analogues and conjugates and chemotherapeutic agents as taught by Bennett et al. and further to incorporate LNA into antisense compounds that allow for increased stability and target affinity given Bennett et al. and Kurreck et al. teach such compounds are capable of inhibition of gene expression and one of skill in the art would have expected to be able to synthesize LNA given Koch et al. details preparation of LNA and incorporation into oligonucleotides.

Thus in the absence of evidence to the contrary, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Applicant's Arguments

Re: Substantial Duplicates

The objection of claims 5, 6, 14, 8, 9, 14, 21, 158 and 162 under 37 CFR 1.75 as being substantial duplicates of each other is withdrawn in response to claim amendments and Applicant's arguments.

Re: Non-statutory Double Patenting

Acknowledgement is made of Applicant's request that the rejection be held in abeyance until allowable matter is indicted in the instant claims, therefore the rejection of claims 3, 5-16, 19-21, 23-38, 45-46, 48-52, 120-124 and 153-169 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of co-pending application 11/272,124 is maintained.

Re: Claim Objections

The objection of claims 23-38 under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim is withdrawn in response to Applicant's argument in the remarks filed 10/12/2007.

The objection of claim 48 as being grammatically incorrect is withdrawn in response to claim amendments filed 10/12/2007.

The rejection of claim 50 is withdrawn in response to Applicant's argument in the remarks filed 10/12/2007.

Re: Claim Rejections - 35 USC § 112

The rejection of claims 3, 5-16, 19-21, 23-38, 45-46, 48-52, 120-124 and 153-169 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn to claim amendments and Applicants arguments filed 10/12/2007.

Claims 19-21 and 160-169 are free of the prior art of record and prior art searched.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Friday between 7-4 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see http://pair-direct.uspto.gov.

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/Kimberly Chong/
Examiner
Art Unit 1635